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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,500	11/14/2000	Christine Van Broeckhoven	B0192/7019	9967

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,500	VAN BROECKHOVEN ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *11-19,21-24 and 30-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,20 and 25-29* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Preliminary Amendment filed June 14, 2000 has been entered. The Preliminary Amendment and Sequence Listing (both paper and computer readable forms) filed August 1, 2002 have been entered.

2. It is noted that the instant application is a 371 of PCT/EP98/08543, filed December 17, 1998. The International Search Report and International Preliminary Examination Report for PCT/EP98/08543 have been received and considered. However, it is further noted that the references cited in the Search Report and Preliminary Examination Report will not be listed on any patent resulting from this application because they were not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO-1449 form, must be filed within the set period for reply to this Office action.

Election/Restriction

3. Applicant's election of Group I, claims 1-10, 20, and 25-32, in the Response to Restriction Requirement filed December 2, 2002, and election of YAC 961_h_9 comprising the repeat of SEQ ID NO: 12, and the primer pair of SEQ ID NOS 13 and 14, in the Response filed March 24, 2003, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 11-19, 21-24, and 33-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no

allowable generic or linking claim. Election was made **without** traverse in the Response of December 2, 2002. Further, as claims 30-32 are drawn to non-elected sequences, those claims are also withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election of the sequences of Figures 15a-b (as recited in, e.g., claim 29) was made **without** traverse in the Response of March 24, 2003.

Priority

5. It is noted that MPEP 1893.03(c) states:

> *Note: a national stage application submitted under 35 U.S.C. 371 may not claim benefit of the filing date of the international application of which it is the national stage since its filing date is the date of filing of that international application. See also MPEP §1893.03(b). Stated differently, since the international application is not an earlier application (it has the same filing date as the national stage), a benefit claim in the national stage to the international application is inappropriate. Accordingly, it is not necessary for the applicant to amend the first sentence of the specification to reference the international application number that was used to identify the application during international processing of the application by the international authorities prior to commencement of the national stage.*
>
> Applicant's claim for benefit of the PCT application of which the instant application is a 371 is improper and should either be:
>
> a) deleted from the specification; or
>
> b) amended to recite, e.g., "this application is a 371 of international application PCT/EP98/08543, filed December 17, 1998."

Oath/Declaration

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it improperly claims priority to the PCT application of which it is a 371. See also paragraph 5, above. As the instant application is a 371of PCT/EP98/08543, a priority claim to the PCT application is not proper.

Specification

7. The amendment filed June 14, 2000 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the incorporation by reference of "the entire contents" of GB 9726804.9 and "all references disclosed herein."

Applicant is required to cancel the new matter in the reply to this Office Action.

8. The disclosure is objected to because it contains multiple embedded hyperlinks and/or other forms of browser-executable code. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

Claim Objections

9. Claim 20 is objected to because of the following informalities: the claim depends from withdrawn claims. Appropriate correction is required.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 and 20 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-10, 20, and 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make

or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

Claims 1-6 are drawn to the use of nucleic acids from particular regions of human chromosome 18q, as well as YAC clones containing said nucleic acids, in identifying genes "associated with a mood disorder or related disorder," and claim 8 is drawn to a method of detecting a gene that employs said clones. Claim 20 is drawn to the use of a probe to said regions of chromosome 18q in methods of detecting mutations or variations "associated with a mood disorder or related disorder." Claims 7 and 9-10 are drawn to methods of identifying a gene or genes in which triplet repeats located in said region of chromosome 18q are detected. Claims 25-29 are drawn to methods of determining the "susceptibility of an individual to a mood disorder or related disorder" in which a polymorphism in said region of chromosome 18q is detected. It is noted that the elected invention is drawn to YAC 961_h_9 comprising the repeat of SEQ ID NO: 12, and the primer pair of SEQ ID NOS 13 and 14.

It is unpredictable as to whether one of skill in the art could make and use applicant's invention. The specification does describe the analysis of a variety of chromosome 18q markers located between D18S51 and D18S61 for an association with bipolar disorder (see entire reference, particularly Table 2). However, the specification further discloses that the highest LOD score obtained for any marker was 2.01 (see pages 31-32). Both the specification and the prior art teach that such a score is not indicative of linkage. Particularly, the specification states at page 4 that "A LOD score of 3 (or likelihood ratio of 1000 or greater) is taken as significant statistical

evidence for linkage," and the definition of LOD score taught by Kahl (page 268 of the *Dictionary of Gene Technology*, VCH, Winheim, 1995) also states that "A LOD score of 3 indicates linkage." Accordingly, given the teachings of specification, in light of both the teachings of the specification and of the art with respect to what LOD score would be indicative of linkage, one of skill in the art would not conclude that any of the nucleic acids or markers encompassed by the claims are associated with bipolar disorder or any other "mood disorder or related disorder." Absent guidance from the specification, one of skill in the art may look to the teachings of the prior art for further clarification and enablement of a claimed invention. However, in the instant case, the prior art is silent with respect to any association between the elected YAC clone and SEQ ID Nos and any type of mood or related disorder. Further, it is noted that in a reference published subsequent to the effective filing date of the instant application (Goossens et al, European Journal of Human Genetics 8:385-388 [2000]), two of the inventors and additional co-authors teach that while the chromosome 18q region encompassed by the instant claims was "previously identified" as having a possible association with bipolar disorder, upon further experimentation, no association between triplet repeats in this region and bipolar disorder was found to exist (see entire reference). Accordingly, in view of the lack of guidance provided by both the specification and the art with respect to an actual association with any mood or related disorder, it is unpredictable as to whether one of skill in the art could practice the claimed invention. Given the high skill level of one of skill in the relevant art, it is clearly within the ability of such an artisan to conduct further experimentation to determine whether molecules encompassed by the

claims are associated with, e.g., a mood disorder other than bipolar disorder. However, the outcome of such experimentation cannot be predicted, and therefore it is unpredictable as to whether any quantity of experimentation would be sufficient to enable one of skill in the art to make and use any molecule encompassed by the claims, as it is unknown as to whether any such molecules or markers associated with mood disorders even exist. Accordingly, it would require undue experimentation to make and use the claimed invention. Further, it is also noted that even if the specification and/or the art were to provide evidence of an association of one or more of the markers encompassed by the claims with bipolar disorder, such evidence would be insufficient to enable the claims in a manner reasonably commensurate with their breadth. The claims encompass numerous disorders embraced by the terminology "mood disorder" and "related disorder;" however, absent evidence of an actual association with disorders other than bipolar disorder, it would be completely unpredictable as to whether an association existed with any other type of mood or related disorder.

13. Claims 4-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite a series of YAC clones. While the specification provides partial sequence information for each of the clones, the specification does not teach, e.g., the complete sequences thereof, or provide sufficient information regarding the structures of these clones such that one of skill in the art could be expected to prepare them without

undue experimentation. Because the sequences of the recited YAC clones are not known and because it is not clear whether they are publicly available or can be reproducibly isolated from nature without undue experimentation, a suitable deposit for patent purposes is required. Without the publicly available deposit of the above clones, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Furthermore, in the event that the deposit is/was made after the effective filing date of the application, Applicant must provide a statement to corroborate that the deposited material is the material specifically identified in the application (see MPEP 2406.02).

If Applicants deposit with an International Deposit Authority is made under the Budapest Treaty, the specification should be amended to recite that the deposit has been made under the Budapest Treaty and to include the deposit accession number, the date of the deposit and the name and address of the depository. For further information concerning deposit practice, Applicants attention is directed to 37 CFR 1.801-1.809 and MPEP 2401-2411.05.

If Applicants deposit with an International Deposit Authority is not made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(A) During the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(B) All restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(C) The deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(D) The deposits were viable at the time of deposit;

and;

(E) The deposits will be replaced if they should ever become non-viable.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-10, 20, and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 and 20 provide for the use of nucleic acids, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 6 is indefinite because it refers to particular types of disorders as classified in a reference manual. The reference manual definitions incorporated into the claim are not provided in either the specification or the claim itself. Accordingly, one of skill in the art cannot ascertain what particular disorders are actually encompassed by the claim.

(It is further noted that essential material may not be incorporated by reference to non-patent publications (see MPEP 608.01(p)).)

Claims 7 and 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Particularly, while the claims are drawn to a method of "identifying at least one human gene," the claimed method includes only a step of detecting triplet repeats; the claims do not actually include a step of identifying a gene.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Particularly, while the claim is drawn to a method of "identifying at least one human gene," the claimed method includes only steps of "fragmentation" of a clone and detection of triplet repeats; the claims do not actually include a step of identifying a gene.

Claims 9-10 are indefinite over the recitation of the limitation "said repeated triplet" because there is insufficient antecedent basis for this limitation in the claims.

Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Particularly, while the claims are drawn to a method of "determining the susceptibility of an individual to a mood disorder or related disorder" the claimed method includes only a step of analyzing a sample of DNA. It is noted that

dependent claims 28-29 are complete in that they indicate how one is determine the presence of susceptibility.

Conclusion

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/872-9306 for regular communications and 703/872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B Johannsen

Diana B. Johannsen
June 27, 2003